

SPECIFICATION

Please amend the following paragraphs of the substitute specification in compliance with 37 CFR 1.121 and 37 CFR 1.57(a) to identify the locations within the provisional application 60/405,352 from which portions of the provisional application were incorporated by reference. The specific incorporated text has been separately been identified in the filing of the substitute specification.

[0007] Prior art means for estimating endothelial dysfunction include the use of cold pressor tests by invasive quantitative coronary angiography "measuring the vasodilator response of coronary arteries to acetylcholine," (from the paragraph entitled "Invasive methods are:" of provisional application 60/405,352) and the injection of radioactive material and subsequent tracking of radiotracers in the blood. These invasive methods are costly, inconvenient, and must be administered by highly trained medical practitioners.

[0008] Noninvasive prior art method for measuring endothelial dysfunction include, the measurement of the percent change and the diameter of the left main trunk induced by cold pressor test with two dimensional echo cardiography, the Dundee step test, laser Doppler perfusion imaging and iontophoresis, high resolution b-mode ultrasound, (from subparagraphs 5 & 6 of the paragraph entitled "Non-invasive methods are:" of provisional application 60/405,352) "detection of vascular conditions using an occlusive arm cuff plethysmograph and detection of medical conditions by monitoring the peripheral arterial tone, in conjunction with the creation of hyperemia by the arm cuff".

[0018] FIG. 4 is an overall system diagram of the invention, in its preferred embodiment (and as illustrated on the cover of provisional application 60/405,352).

[0030] FIG. 4 is an overall system diagram of an embodiment of the invention (as stated in the "Brief Description of the Drawings" for FIGURE1 for provisional application 60/405,352.) Hyperemia is simulated by creating an occlusion of the target artery (by inducing cuff pressure on arm, wrist, finger or leg) for some time and then suddenly releasing the occlusion. The changes in the

arterial blood flow are monitored before the occlusion and then after the release of occlusion. Different techniques may be used to determine the blood flow through the arteries and may include but are not limited to pulse oximetry, temperature measurements, piezoelectric sensors or auditory sensors. These changes are then used to predict the endothelium dysfunction present if any.

[0031] In one embodiment, a method for self administered endothelial function evaluation is provided comprising: creation of occlusion on the arm, leg, wrist or finger of a person in order to block the arterial blood flow, maintaining of the said occlusion for predetermined time at the predetermined pressure, removing the occlusion after predetermined period, monitoring of the changes in the oxygen content of the blood, temperature of finger tip or the blood flow rate, and prediction of endothelial function (EF) from the analysis of the above parameters. (See claim 2 of provisional application 60/405,352)

[0032] In one embodiment, monitoring of the changes in the oxygen content of the blood is provided by a pulse oximeter connected to the tip of a finger to continuously monitor the oxygen content of the blood in order to predict endothelial function (EF). In another embodiment, temperature sensors are placed on the tip of the finger, to monitor the blood flow and predict the EF from that. In one embodiment, monitoring is provided by two or more sensors separated by some known distance are placed on the forearm of the person when the occlusion is created in the arm, to determine the blood flow rate. The sensors may be piezo electric sensors, micro phone, pressure etc. (See claims 3, 4 and 5 of provisional application 60/405,352)

[0033] In one embodiment, monitoring is provided by a photoplethysmograph apparatus placed near the finger to monitor the blood flow. In another embodiment, two or more sensors separated by some distance are placed on the arm or the hand and the impedance between them is continuously monitored. This in turn gives the endothelial function. (See claims 6 and 7 of provisional application 60/405,352)

[0034] In one embodiment, the blood flow is measured with the help of a Magnetohydrodynamic Acoustic-Resonance Near-Infrared (MARENIR) technique. In another embodiment, blood flow and the changes in the artery dimensions are monitored by a combined Ultrasound-Doppler technique. (See claims 8 and 9 of provisional application 60/405,352)

[0035] In one embodiment, hyperemia is simulated by creating an occlusion of the target artery (by inducing cuff pressure by a cuff on arm, wrist, finger or leg) for some time and then suddenly releasing the occlusion. Blood flow is monitored over the course of time right from before the creation of occlusion till the blood flow is normalized after the removal of the occlusion, in order to exactly predict the EF. In one embodiment, blood flow and the change in the blood flow are plotted against the time. These two graphs are further analyzed to give more accurate value of the endothelial function. In one embodiment, a self-administered endothelial function assessment system is provided which gives a "Risk factor score" to the patient at the end of the test, indicating the amount of risk the user has. (See claims 10, 11 and 12 of provisional application 60/405,352)